Adv.

Pollen Antigens
Lederle

FOR

HAY FEVER

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Hay-Fever

ITS DIAGNOSIS AND
TREATMENT WITH

Pollen Antigens*

Illustrated

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Lederle Antitoxin Laboratories
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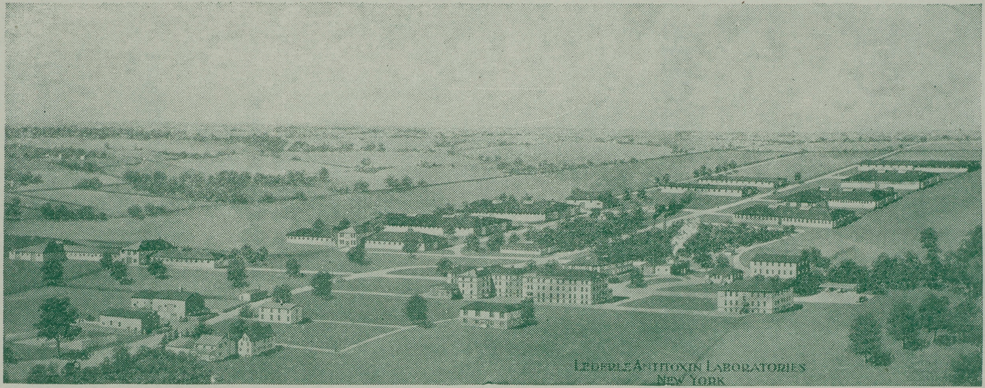
**The name "Pollen Antigen" denotes the product of the Lederle Antitoxin Laboratories*



Lederle Antitoxin Laboratories, Pearl River, Rockland County, N. Y.
where the original work of preparing glycerolated pollen antigens in stable and standardized solution was carried out in 1914.

Preface

THE object of this little book is to give the busy practitioner the important facts concerning the pollens that cause hay-fever; to explain to him briefly the approved methods of making diagnostic tests and administering the pollen treatment; and to provide him with a handy reference so that he may readily know the various pollens causing hay-fever at different seasons of the year in his own locality.

A special study has been made of the botanical flora in each section of the country, and the hay-fever pollens of primary and secondary importance in the different geographical areas have been tabulated according to their season of pollination.

The line drawings of cocklebur (page 27), giant ragweed (page 26), marsh elder (page 28), mugwort (page 26), ragweed (page 22), sage brush (page 28), sheep sorrel (page 13), spiny amaranth (page 18), Western ragweed (page 3), Western water hemp (page 14), and yellow dock (page 15), are from ADA GEORGIA'S ''Manual of Weeds,'' published by the Macmillan Company, New York. We wish to express here our thanks for the kind permission to reproduce these copyrighted drawings. The photoengravings of the grasses (pages 7, 10, 11, 12, 16 and 19) are from Farmer's Bulletin ''Important Cultivated Grasses,'' published by the United States Department of Agriculture, through whose courtesy they are here reproduced. The line drawings of pasture sage and green sage

(pages 17 and 18) are from the monograph by HALL and CLEMENTS entitled, "The North American Species of Artemisia, Chrysothamnus and Atriplex," published by the Carnegie Institution of Washington, through whose courtesy they are here reproduced. The other drawings are original and were made especially for this booklet.

LEDERLE ANTITOXIN LABORATORIES.

January
1926

Hay-Fever

CHAPTER I

Pollen Antigens (Lederle)

In 1914, researches conducted in the Lederle Antitoxin Laboratories resulted in the perfection of glycerolated pollen antigens in stable and standardized solution. The physician for the first time was thus afforded a means for the scientific treatment of his hay-fever patients.

Pollen Antigens (Lederle) are prepared by extracting the mature pollen grains in 66⅔ per cent glycerol and 33⅓ per cent saturated sodium chloride solution. This method of preparing Pollen Antigens (Lederle) has been continuously used for twelve years, during which time it has proved to produce *uniformly potent and stable pollen antigens.* These antigenic solutions are standardized against antipollen serum by the complement fixation method which accurately determines the antigenic activity of the pollen protein. *This ensures an active and potent product.*

Sweet Vernal Grass
(Anthoxanthum odoratum)

Wind-Borne Pollens

Hay-fever is a condition of hypersensitiveness to pollen proteins and is produced primarily by the inhalation of wind-borne pollens. However, only those wind-borne pollens that are inhaled during normal respiration cause true hay-fever. Thus, SCHEPPEGRELL[1] says:

> "While there are many plants whose pollen may cause the hay-fever reaction when applied to the nostrils, *only pollens which float in the air and can reach the nostrils in the course of normal respiration are responsible for true hay-fever.*"

This fact was definitely established[2] by means of atmospheric-pollen plates which were exposed daily, during the hay-fever season, at various stations of the American Hay-Fever Prevention Association and also near the residences of the hay-fever patients. The plates were coated with glycerin and exposed for periods of twenty-four hours and then taken to the laboratory, stained, examined microscopically and the pollens identified.

Oak blossoms
(Quercus alba)

Characteristics of Hay-Fever Pollens

Pollens are carried from one plant to another

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[1] SCHEPPEGRELL, W.: Hay-Fever and Hay-Fever Pollens, *Arch. Int. Med.*, June 15, 1917, p. 959.

[2] SCHEPPEGRELL, W.: Hay-Fever and Its Relation to 100 of the Most Common Plants, Trees and Grasses, *Med. Rec.*, Aug. 11, 1917, p. 230.

either through the agency of the wind or by insects. The principal and most important fact in connection with hay-fever is that *only those pollens which are carried by the wind and which are therefore in the air can cause true hay-fever.* For complete list of hay-fever plants, see pages 40 and 41.

Western Ragweed
(Ambrosia psilostachya)

Wind-pollinated plants *are distinguished by their inconspicuous flowers which are devoid of scent or odor; their pollen is shed in large amounts and is light and buoyant.*

Insect-Borne Pollens

On the other hand, insect-pollinated plants are characterized by their bright-colored, conspicuous flowers which have a sweet scent or odor; their pollen is heavy and viscid and is shed very sparingly. *Insect-pollinated plants are not an important factor in hay-fever,* because their pollen is never present in the atmosphere in sufficient amounts to reach the nostrils in the course of normal respiration.

The fact that *true hay-fever is caused by the inhalation of wind-borne pollens only,* eliminates a long list of insect-pollinated plants and trees which are popularly supposed to cause hay-fever.

Lambs Quarters
(Chenopodium album)

Harmless Plants and Trees

Johnson Grass
(Sorghum halepense)

These insect-pollinated plants comprise alfalfa, aster, chrysanthemum, clover, crimson rambler, dahlia, dandelion, goldenrod, honey-suckle, jonquil, lilac, lily-of-the-valley, mountain laurel (rose bay or oleander), roses, rose of Sharon, spirea, sugar beet, sunflower, white daisy, and yellow daisy. The insect-pollinated trees which are harmless in hay-fever include the common fruit trees (apple, apricot, peach, pear, plum) and most of the ornamental flowering trees, such as catalpa, crepe, myrtle, dogwood, locust and magnolia.[3] Moreover, SCHEPPEGRELL states that several trees whose pollen is wind-borne are negative in hay-fever, including the arbor vitæ, cypress, fir, hemlock, pine and spruce.

Hay-fever in the late spring and early summer is often erroneously designated ''rose cold'' or ''rose fever.'' Such a name is a misnomer, for hay-fever at this time of year is not caused by rose pollen but by pollen from the grasses. In like manner, fall hay-fever is popularly attributed to pollen of the goldenrod,[4] while in reality it is caused in the vast majority of cases by ragweed.

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[3] SCHEPPEGRELL, W.: Hay-Fever and Asthma, Lea and Febiger, Philadelphia, 1922.

[4] SCHEPPEGRELL, W.: The Goldenrod Is Not Responsible for Hay-Fever, *U. S. Pub. Health Reports*, July 21, 1916.

There are certain insect-pollinated plants whose pollen will undoubtedly produce hay-fever symptoms if directly inhaled, but *such pollens are never found in the air in any great quantity and so are practically not a factor in the hay-fever situation.* The pollen of insect-pollinated plants may precipitate an attack of hay-fever under exceptional circumstances—such, for example, as where the flowers are deliberately smelled as might be done particularly by children, or where the plants are grown in great profusion in close contact with the patient, or even in some cases where the flowers are used for room decoration. But such symptoms would not long persist.

Cottonwood blossoms
(Populus macdougali)

Pollens of Cereal Grains

The pollen of corn, in spite of its toxicity, is rarely responsible for hay-fever; because its size is so great that it cannot travel far; so that only by close proximity to a corn field can hay-fever be induced. Rye and wheat also have large pollen grains and, therefore, are of little practical importance as a cause of hay-fever. The cereals, however, including rye, wheat, oats and corn, may constitute a local cause of hay-fever in some States.

CHAPTER II

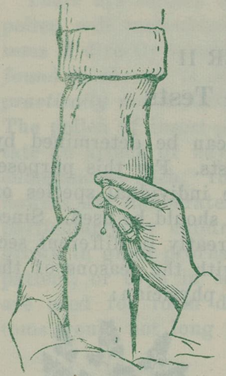
Diagnostic Tests

Sensitiveness to pollens can be determined by applying diagnostic skin tests. For this purpose, extracts prepared from the individual species of pollens that cause hay-fever should be used. Since the botanical flora varies greatly in different sections of the country and with the seasons of the year, it is essential for the physician:

1. *To ascertain the exact date when his patient's hay-fever symptoms appear.*
2. *To acquaint himself with the hay-fever plants most common in the locality where his patient lives.*

This information will be found on pages 30 to 39, where the hay-fever plants of individual states are listed. The tables on these pages contain in the left-hand column the common and botanical names of the plants, and in the right-hand column are given the months of the year during which the individual plants bloom. These months correspond to the time when the hay-fever symptoms occur.

Orchard Grass
(Dactylis glomerata)



Diagnostic Skin Test
(Puncture Method)
Expelling Pollen Diagnostic from capillary tube to forearm.

For example, a hay-fever patient living in Massachusetts has symptoms of hay-fever from May to September. This corresponds to the pollinating season of June grass. Therefore, by applying a June grass skin test, if a positive reaction occurs such a patient should be given the desensitizing treatment with June grass pollen antigen.

How to Make a Skin Test

Puncture Method: Cleanse the flexor surface of forearm with alcohol or ether. After evaporation of the alcohol or ether, place a drop of Pollen Diagnostic upon the cleansed skin, by expelling it from a glass capillary tube.

Holding the sterile needle nearly parallel with the skin, make about six oblique pricks or shallow punctures through the epidermis by pressing the point of the needle through the drop of Diagnostic. Confine the punctures to an area not more than one-eighth (1/8) of an inch in diameter.

Sufficient Diagnostic to produce a positive reaction (urticarial wheal) in susceptible persons will be carried beneath the skin by these multiple punctures. The surplus Diagnostic on the surface of the skin may be wiped off immediately, thus making it possible to observe the reaction as it is forming.

A positive reaction consisting of an urticarial wheal or white elevation of the skin will appear in

sensitive persons in 15 to 30 minutes. When it begins to form, the wheal is often irregular in outline, with many radiating portions. These gradually coalesce, leaving a larger irregular wheal.

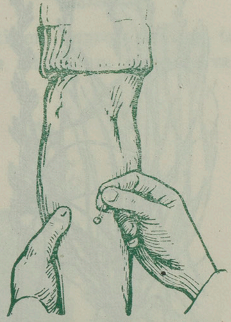
Scratch Method: This is not as delicate a test as the puncture method, and does not as readily permit of observing the formation of the urticarial wheal.

Cleanse the skin as above described, and, with sterile needle, make a small scarification about one-eighth (1/8) of an inch long through the Diagnostic material on the flexor surface of the forearm. A second scarification may be made as a control. At the end of one-half hour, wipe off the Diagnostic and note the reaction, comparing it with the control.

Interpretation of Skin Reactions

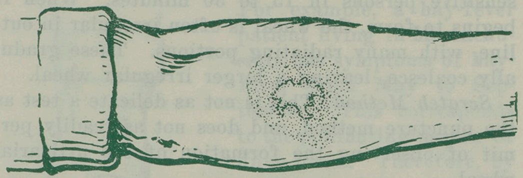
The pollens which are not the cause of the patient's hay-fever will produce no reaction. A *positive reaction* consists of an urticarial wheal or white raised area of the skin, which looks like a hive or mosquito bite surrounding the scarification. The wheal is usually surrounded by a zone of redness.

The degree of the reaction is determined entirely by the size and shape of the urticarial wheal. The surrounding zone of erythema or redness may be disregarded. For a reaction to be considered positive, there must be a true urticarial wheal. The greater the ir-



DIAGNOSTIC SKIN TEST
(Puncture Method)

Making multiple punctures with needle point pressed through drop of Pollen Diagnostic.



Diagnostic Skin Test

Positive pollen reaction, showing urticarial wheal irregular in outline with radiating portions and surrounded by an erythematous area.

Perennial Rye Grass
(Lolium perenne)

regularity in outline of the urticarial wheal, the greater is the sensitiveness of the patient to that particular pollen. Thus, an urticarial wheal with pseudopods (irregular, radiating portions), is of greater significance than a wheal having a more or less regular outline without pseudopods. The swollen area (urticarial wheal) may be as large as one to two inches (25 to 50 millimeters) in diameter, but more often is about ⅝-inch (15 millimeters). It is often associated with intense itching of the skin.

This skin test indicates which pollens are the cause of hay-fever in the individual case. *Several skin tests should be made, using those pollens which are*

known to be most prevalent in the atmosphere at the season when the patient experiences the most severe hay-fever symptoms. If the patient is affected by several pollens (as indicated by positive skin reactions produced by more than one pollen), the degree of reactions will distinguish between the pollens that affect the patient only slightly and those that are harmful and are responsible for the hay-fever symptoms. It is important to determine by these skin tests which pollen is the principal offender in causing the hay-fever symptoms, and treatment should be given with the pollen antigen corresponding to that pollen which gives the maximum positive reaction in the skin test.

June Grass
(Blue Grass, *Poa pratensis*)

Mountain Cedar
(*Juniperus sabinoides*)

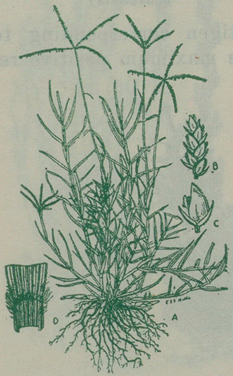
CHAPTER III

Pollen Treatment

CLOWES was the first to report a definite method of vaccination against hay-fever in this country; but to KOESSLER must be given the credit for placing the method of desensitization against hay-fever on a scientific basis.

Glycerolated Pollen Antigens (Lederle)

With the end in view of devising some method for preparing a uniformly stable product, we extracted pollen by various methods [5] and succeeded in preparing uniformly stable pollen antigens [6] by extracting the pure, mature pollen grains in 66⅔ per cent glycerol and 33⅓ per cent saturated sodium chloride solution. Such glycerolated pollen antigens proved to be remarkably stable and more potent than those obtained by any other method of extraction, for no loss in antigenic properties could be detected in the glycerolated pollen antigens after being stored in the icebox for twenty-two months.



Bermuda Grass
(Capriola dactylon)

[5] CLOCK, R. O.: Comparative Value of the Methods of Preparing Pollen Antigen. *J. Infec. Dis.*, Dec., 1917, p. 523.

[6] CLOCK, R. O.: A Stable Pollen Antigen. *J. Infec. Dis.*, Oct., 1917, p. 387.

Standardization

By means of the complement fixation method, we accurately standardized Pollen Antigens (Lederle) against antipollen serum,[7] definitely determining the amount of antigenically active protein in the extract. This ensures their antigenic activity and provides for accurate dosage; for the protein in the glycerolated pollen antigens is preserved by the glycerol from autolytic deterioration, so that the original standardization is permanent.

The investigations of the United States Public Health Service[8] into the status of preventive treatment of seasonable hay-fever included an analysis of the various methods of preparing and testing pollen extracts. It will be of interest to physicians that this investigation confirms the work originally carried out in the Lederle Antitoxin Laboratories; also that the method for the preparation and testing of pollen antigens developed in the Lederle Antitoxin Laboratories and reported by Dr. Clock was found satisfactory, as shown by the following excerpt from the report of the Public Health Service expert:

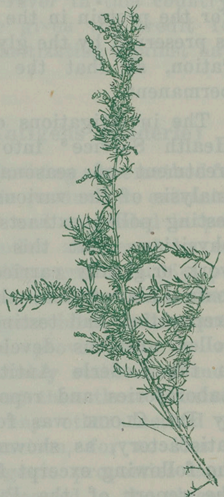
"Clock is deserving

Sheep Sorrel
(Rumex acetosella)

[7] Clock, R. O.: Antipollen Serum for Standardization of Pollen Antigen, *J. Infec. Dis.*, Jan., 1918, p. 80.

[8] Bernton, H. S.: Treatment of Seasonable Hay-Fever and Some Possible Causes of Failure, *Jour. A. M. A.*, May 5, 1923, p. 1301.

Western Water Hemp
(Acnida tamariscina)



Shad Scale
(Atriplex canescens)

of much credit for calling attention to the fact that chemical analysis fails to demonstrate the antigenic qualities of pollen extracts. Such analysis reveals only the amount of pollen protein present in solution. Clock has shown that a practical method of determining the antigenic properties of pollen extract is by means of the complement fixation test. . . . He has, furthermore, devised a method of preparing a stable antigen by the use of concentrated salt solution and glycerol. Pollen extracts, prepared by his method, have remained for fourteen months without loss of complement binding capacity. With his glycerolated pollen antigen Clock obtained relief from symptoms in 84 per cent of 1,578 cases. Our experience is confirmatory of Clock's observations."

Yellow Dock
(Rumex crispus)

Prophylactic (Pre-seasonal) Treatment

(A) For the Average Case

The importance of pre-seasonal pollen treatment cannot be too strongly emphasized. For successful desensitization, it is essential that the prophylactic treatment with Pollen Antigen (Lederle) be started about five weeks before the date of the expected attack of hay-fever. Having determined by the diagnostic skin test the pollen to which the person is most sensitive, pre-seasonal treatment is carried out by giving a

Timothy
(Phleum pratense)

series of fifteen doses of Pollen Antigen (Lederle) prepared from the corresponding pollen that gave the maximum positive reaction in the diagnostic skin test.

The antigen is administered *subcutaneously,* preferably in the arm over the insertion of the deltoid muscle. In making the subcutaneous injection, care should be used to keep the needle from penetrating a subcutaneous vein; otherwise the sudden entry of even a small amount of foreign protein (pollen antigen) may produce an anaphylactoid shock in a person sensitive to pollen.

The interval between each dose of the pollen antigen is usually 48 hours; a convenient plan being to administer the antigen three times a week. For years, this plan has yielded satisfactory results in the average case.

The pre-seasonal treatment should be finished on about the date of the usual onset of hay-fever symptoms, in order that the person may be in a condition of maximum desensitization during the pollinating season of the plants.

(B) Hypersensitive Cases

A few persons (less than 1% of the cases reported) may be unusually sensitive to pollen protein, so that in the course of the pollen treatment some dose may produce a severe reaction. Such persons may often be successfully treated by injecting only one-half or one-quarter of each of the remaining doses. These fractional doses will usually be well tolerated if given *daily*. If, however, the reaction from any dose is marked, it is advisable to wait until it subsides before proceeding with the treatment. After dose 15 has been reached and a fraction of it administered, the pollen treatment should be continued by injecting increasing amounts of dose 16 until finally the full amount of dose 16 is given.

In order to control the symptoms of protein reaction in hypersensitive persons, it is advisable to combine about 5 minims of epinephrin (1:1,000 solution) with each dose of pollen antigen. This can readily be done by drawing up the desired amount of epinephrin into the syringe containing the diluted pollen antigen. When administering the higher doses of pollen antigen (doses 11 to 15) it may be advisable to combine with

Pasture Sage
(Artemisia frigida)

Green Sage
(Artemisia campestris)

Spiny Amaranth
(Amaranthus spinosus)

each dose about 10 minims of the epinephrin solution. By constricting the arterioles, epinephrin slows absorption of the foreign protein (pollen antigen) and hence tends to minimize protein reactions.

(C) Refractory Cases

In treating refractory cases—that is, those persons who in previous years have not derived entire relief from their hay-fever symptoms—some clinicians prefer to start the pollen treatment *three weeks* before the hay-fever season, and to *administer a dose of pollen antigen daily.* If any dose causes a marked local reaction which persists for 24 hours, the next dose is delayed for another day.

After the regular treatment of 15 doses has been given at approximately *daily intervals,* five doses of the special dose 16 are given at intervals of about three days (twice weekly), in order to give the patient the maximum protection during the height of the pollinating season.

Clinicians report that *by using this intensive method of treatment,* the doses are as well if not better tolerated than when longer intervals between doses are used; and that *a higher percentage of completely protected cases is obtained.*

Redtop
(Agrostis palustris)

Ash blossoms
(Fraxinus toumeyi)

Treatment of Attack

Pre-seasonal treatment yields by far the most satisfactory results and the physician should always impress upon his patient the advisability of taking the pollen treatment in advance of the hay-fever season. Nevertheless, many patients do not apply to their physician for relief from hay-fever symptoms until the actual attack of hay-fever has already begun.

In treating an attack of hay-fever, it is important always to start with dose 1; for it must be borne in mind that the patient is already absorbing pollen from the atmosphere and if the higher doses of pollen antigen are used at first, the hay-fever symptoms may be temporarily aggravated and the patient's condition rendered worse instead of better.

The doses may be progressively increased and as many doses given as may be needed to control the attack. It may be necessary to administer the complete series of fifteen doses before the symptoms entirely disappear in some patients. Others may be benefited by three or four doses, with complete cessation of hay-fever symptoms after the eighth or ninth dose.

Usually, the doses may be given every day until a marked local reaction is produced; after that at intervals of two days. If any dose causes a severe reaction, as shown by an increase in the hay-fever symptoms, it is advisable to inject only one-

half or even one-quarter of each of the subsequent doses, depending upon the degree of reaction.

When used during the attack of hay-fever, Pollen Antigen (Lederle) has in many hundreds of cases alleviated the conditions, as indicated by the symptoms being milder and the attack shorter. The physician can do much to advance the science of the pollen treatment of hay-fever if he will use the opportunity afforded him, when administering pollen treatment during an attack of hay-fever, to impress his patient with the possibility of greater benefit to be derived from preseasonal treatment in the following year.

Careless Weed
(Amaranthus palmeri)

Desensitization Not Permanent

Since hay-fever is not an infectious disease but rather a state of hypersensitiveness to pollen protein, it is impossible to produce a true immunity against it. COOKE and others have pointed out that desensitization in hay-fever is not permanent or stable; freedom from symptoms lasts only as long as the antigen remains in combination with the tissue-antibodies. The state of desensitization is probably complete for only a few weeks after completion of the antigen treatment and gradually diminishes. Hence, it is essential to administer Pollen Antigen (Lederle) each year in order to protect the person from hay-fever.

Slender Ragweed
(Franseria tenuifolia)

Ragweed
(Ambrosia elatior)

CHAPTER IV
Dosage

In the application of desensitization to hay-fever, it is important to *always begin with small doses.* The experiments of Weil have proved that small amounts of proteins injected repeatedly will desensitize against small amounts, whereas the injection of large amounts of proteins will desensitize against large amounts. Hence, the method of gradually increasing the dose is theoretically correct and the person must be rendered refractory to large doses about the time of the expected attack of hay-fever. In its practical application this method has been proved to be correct. The scheme of dosage which we adopted for the glycerolated pollen antigens consists of 15 doses of a gradually increasing number of pollen units; the pollen unit having been established by Noon, who defined it as the equivalent of one millionth gram of pollen.

Southwestern Ragweed
(Ambrosia aptera)

The actual strength of the various doses is as follows:

	Dose 1	contains	2½	pollen	units
	Dose 2	contains	5	pollen	units
	Dose 3	contains	10	pollen	units
	Dose 4	contains	20	pollen	units
	Dose 5	contains	25	pollen	units
	Dose 6	contains	30	pollen	units
	Dose 7	contains	50	pollen	units
	Dose 8	contains	75	pollen	units
	Dose 9	contains	100	pollen	units
	Dose 10	contains	150	pollen	units
	Dose 11	contains	250	pollen	units
	Dose 12	contains	375	pollen	units
	Dose 13	contains	500	pollen	units
	Dose 14	contains	750	pollen	units
	Dose 15	contains	1000	pollen	units
SPECIAL:	Dose 16	contains	1500	pollen	units

This higher dose 16 is provided for additional treatment of persons who are less sensitive to pollen protein and who are, therefore, more refractory to the desensitizing treatment; also when higher dosage than is contained in the complete series of 15 doses is desired.

Rabbit Bush
(Franseria deltoidea)

Pollen Antigens (Lederle) are supplied undiluted; each vial of glycerolated antigen contains an accurately measured dose and is accompanied by a vial of diluent. The dilution is made by transferring (with a sterile syringe) the diluent to the vial containing the antigen. The physician makes the dilution at the moment of making the injection.

CHAPTER V
Clinical Results

Pollen Antigens (Lederle) were first prepared in 1914 and were described[9] in 1917. They have been used by physicians in all parts of the United States as well as Canada, Central America, Cuba, Porto Rico, South America, New Zealand, Australia, Canary Islands, Philippine Islands, China, British Isles, Norway, Sweden, Denmark, Holland, Belgium, France, Italy, Czecho-Slovakia, Bulgaria, South Africa, Mexico, New Zealand, Barbadoes, Bermuda, Turkey, Mesopotamia, etc.

It has been clinically demonstrated that hay-fever can, in many cases, be prevented or alleviated by treatment with the glycerolated pollen antigen prepared from the particular pollen to which the person is sensitive. In 1922, CLOCK reported[10] an analysis of 1,578 clinical reports from physicians in all sections of the United States who had used the glycerolated pollen antigen during five consecutive years. This analysis shows an average protection or relief from hay-fever symptoms in 84 per cent of cases with a re-

Russian Thistle
(Salsola pestifer)

[9] CLOCK, R. O.: A Stable Pollen Antigen, *J. Infec. Dis.*, Oct., 1917, p. 387.

[10] CLOCK, R. O.: Hay-Fever and Its Treatment with Glycerolated Pollen Antigen, *Jour. Med. Soc., New Jersey*, March, 1922, p. 63.

Mugwort
(Artemisia vulgaris)

Giant Ragweed
(Ambrosia trifida)

markable uniformity of favorable results each year in every locality.

During the past twelve years, Pollen Antigens (Lederle) have been used for the treatment of hay-fever in more than 125,000 cases. When the prophylactic series (doses 1 to 15) of pollen antigen has been administered, beginning about five weeks before the date of the usual attack of hay-fever, the results reported as favorable showed complete freedom from symptoms of hay-fever; or in those cases in which hay-fever did develop, the symptoms persisted for a few days only and were mild in character. Favorable results were also manifested in the possibility of the patient remaining in his home town and at his usual work during the hay-fever season for the first time in years.

Cocklebur
(Xanthium canadense)

Sage Brush
(Artemisia tridentata)

Marsh Elder
(*Iva ciliata*)

Advantages of Pollen Antigen (Lederle)

Pre-seasonal injections of glycerolated pollen antigen offers the best means of any method thus far devised for the preventive treatment of hay-fever. It is not necessary to forsake one's business during the summer months and stay outside the zone of the offending plants. Glycerolated pollen antigen permits the successful desensitization of hay-fever sufferers, allowing them to transact business without discomfort in their usual surroundings.

Redroot Pigweed
(Amaranthus retroflexus)

Pollen Antigen (Lederle) possesses these points of superiority:

1. Prepared from the whole grains of mature dried pollen, thus providing the maximum antigenic qualities of the pollen in the extract.

2. Accurately standardized against antipollen serum by the complement fixation method which definitely determines the antigenic activity, thus ensuring an active and potent product.

3. Uniformly stable, being protected against autolytic deterioration of the pollen protein by 66⅔ per cent glycerol, so that the original strength of the antigen is maintained for a long period.

4. Have yielded uniformly favorable results over a period of twelve consecutive years.

CHAPTER VI

Causes and Seasons of Hay-Fever

United States and Canadian Provinces

The hay-fever seasons vary in different sections of the country, being dependent upon the flowering periods of the various hay-fever plants which are governed by climatic conditions. In the following tables, the most important pollens from a hay-fever standpoint are shown in heavy face type, as well as being indicated by an asterisk(*). The others are usually of secondary or minor importance, except possibly in certain localities where they may assume primary importance.

New England States

(Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, Connecticut)

(Canadian Provinces: Nova Scotia, Prince Edward Island, New Brunswick and Quebec)

NAME	TIME OF BLOOM (Hay-Fever Season)
Black Walnut *(Juglans nigra)*	March - May
Cottonwood *(Populus macdougali)*	April - May
Oak *(Quercus alba)*	April - May
Sweet Vernal Grass *(Anthoxanthum odoratum)*	April - July
Orchard Grass *(Dactylis glomerata)*	April - Aug.
Sheep Sorrel *(Rumex acetosella)*	May - July
Yellow Dock *(Rumex crispus)*	May - July
***June Grass** *(Poa pratensis)*	**May - Sept.**
***Timothy** *(Phleum pratense)*	**June - Aug.**
***Redtop** *(Agrostis palustris)*	**June - Sept.**
Lambs Quarters *(Chenopodium album)*	June - Sept.
Cocklebur *(Xanthium canadense)*	July - Sept.
***Ragweed** *(Ambrosia elatior)*	**Aug. - Oct.**
Giant Ragweed *(Ambrosia trifida)*	Aug. - Oct.

*Pollens of primary importance.

For index of States and Provinces see page 44.

Eastern States

(New York, New Jersey, Pennsylvania, Delaware, Maryland, Virginia, West Virginia)

NAME	TIME OF BLOOM (Hay-Fever Season)
Black Walnut *(Juglans nigra)* - - -	March - May
Cottonwood *(Populus macdougali)* -	April - May
Oak *(Quercus alba)* - - - - - - -	April - May
Sweet Vernal Grass *(Anthoxanthum odoratum)* - - - - - - - - - -	April - July
Orchard Grass *(Dactylis glomerata)* -	April - Aug.
Sheep Sorrel *(Rumex acetosella)* - -	May - July
Yellow Dock *(Rumex crispus)* - - -	May - July
***June Grass** *(Poa pratensis)* - - -	**May - Sept.**
***Timothy** *(Phleum pratense)* - - -	**June - Aug.**
***Redtop** *(Agrostis palustris)* - - -	**June - Sept.**
Lambs Quarters *(Chenopodium album)*	June - Sept.
Cocklebur *(Xanthium canadense)* - -	July - Sept.
***Ragweed** *(Ambrosia elatior)* - - -	**Aug. - Oct.**
Giant Ragweed *(Ambrosia trifida)* - -	Aug. - Oct.

*Pollens of primary importance.

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Southern States

(North Carolina, South Carolina, Georgia, Florida, Alabama, Mississippi, Tennessee, Arkansas, Louisiana, Oklahoma, Texas)

NAME	TIME OF BLOOM (Hay-Fever Season)
Mountain Cedar *(Juniperus sabinoides)* The mountain cedar is found over a considerable part of Texas, Mexico and part of New Mexico.	Dec. - Feb.
Cottonwood *(Populus macdougali)* - -	Feb. - April
Black Walnut *(Juglans nigra)* - - -	March - May
Oak *(Quercus alba)* - - - - - - -	April - May
Sweet Vernal Grass *(Anthoxanthum odoratum)* - - - - - - - - - - -	April - July
Orchard Grass *(Dactylis glomerata)* -	April - Aug.
Perennial Rye Grass *(Lolium perenne)*	May - July
Sheep Sorrel *(Rumex acetosella)* - -	May - July
Yellow Dock *(Rumex crispus)* - - -	May - July
***June Grass** *(Poa pratensis)* - - -	**May - Sept.**
***Bermuda Grass** *(Capriola dactylon)*	**May - Sept.**
***Timothy** *(Phleum pratense)* - - -	**June - Aug.**
***Redtop** *(Agrostis palustris)* - - -	**June - Sept.**
Spiny Amaranth *(Amaranthus spinosus)*	June - Sept.
Lambs Quarters *(Chenopodium album)*	June - Sept.
***Johnson Grass** *(Sorghum halepense)*	**June - Oct.**
Cocklebur *(Xanthium canadense)* - -	July - Sept.
Redroot Pigweed *(Amaranthus retroflexus)* - - - - - - - - - - -	July - Sept.
***Ragweed** *(Ambrosia elatior)* - - -	**Aug. - Oct.**
***Giant Ragweed** *(Ambrosia trifida)* -	**Aug. - Oct.**
Marsh Elder *(Iva ciliata)* - - - -	Aug. - Oct.

*Pollens of primary importance.

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Central States

(Kentucky, Ohio, Indiana, Michigan, Illinois, Wisconsin)

(Canadian Province: Ontario)

NAME	TIME OF BLOOM (Hay-Fever Season)
Black Walnut *(Juglans nigra)*	March - May
Cottonwood *(Populus macdougali)*	April - May
Oak *(Quercus alba)*	April - May
Sweet Vernal Grass *(Anthoxanthum odoratum)*	April - July
Orchard Grass *(Dactylis glomerata)*	April - Aug.
Sheep Sorrel *(Rumex acetosella)*	May - July
Yellow Dock *(Rumex crispus)*	May - July
***June Grass** (Blue Grass, *Poa pratensis)*	**May - Sept.**
***Timothy** *(Phleum pratense)*	**June - Aug.**
***Redtop** *(Agrostis palustris)*	**June - Sept.**
Spiny Amaranth *(Amaranthus spinosus)*	June - Sept.
Lambs Quarters *(Chenopodium album)*	June - Sept.
Annual Saltbush *(Atriplex Wrightii)*	July - Sept.
Redroot Pigweed *(Amaranthus retroflexus)*	July - Sept.
Cocklebur *(Xanthium canadense)*	July - Sept.
Russian Thistle *(Salsola pestifer)*	July - Sept.
***Ragweed** *(Ambrosia elatior)*	**Aug. - Oct.**
***Giant Ragweed** *(Ambrosia trifida)*	**Aug. - Oct.**
Western Ragweed *(Ambrosia psilostachya)*	Aug. - Oct.

*Pollens of primary importance.

For index of States and Provinces see page 44.

Middle Western States

(Minnesota, Iowa, Missouri, North Dakota, South Dakota, Nebraska, Kansas)

(Canadian Province: Manitoba)

NAME	TIME OF BLOOM (Hay-Fever Season)
Black Walnut *(Juglans nigra)*	March - May
Cottonwood *(Populus macdougali)*	March - May
Oak *(Quercus alba)*	April - May
***Sweet Vernal Grass** *(Anthoxanthum odoratum)*	**April - July**
Orchard Grass *(Dactylis glomerata)*	April - Aug.
Sheep Sorrel *(Rumex acetosella)*	May - July
Yellow Dock *(Rumex crispus)*	May - July
***June Grass** (Blue Grass, *Poa pratensis*)	**May - Sept.**
***Timothy** *(Phleum pratense)*	**June - Aug.**
Redtop *(Agrostis palustris)*	June - Sept.
Spiny Amaranth *(Amaranthus spinosus)*	June - Sept.
Lambs Quarters *(Chenopodium album)*	June - Sept.
Annual Saltbush *(Atriplex Wrightii)*	July - Sept.
Redroot Pigweed *(Amaranthus retroflexus)*	July - Sept.
Sage Brush *(Artemisia tridentata)*	July - Sept.
Cocklebur *(Xanthium canadense)*	July - Sept.
Russian Thistle *(Salsola pestifer)*	July - Sept.
Summer Cypress *(Kochia scoparia)*	July - Oct.
Green Sage *(Artemisia campestris)*	July - Oct.
Pasture Sage *(Artemisia frigida)*	July - Oct.
Western Water Hemp *(Acnida tamariscina)*	July - Oct.
***Ragweed** *(Ambrosia elatior)*	**Aug. - Oct.**
***Giant Ragweed** *(Ambrosia trifida)*	**Aug. - Oct.**
***Western Ragweed** *(Ambrosia psilostachya)*	**Aug. - Oct.**
Marsh Elder *(Iva ciliata)*	Aug. - Oct.

*Pollens of primary importance.

For index of States and Provinces see page 44.

Rocky Mountain States

(Montana, Wyoming, Colorado, Utah, Idaho)

(Canadian Provinces: Saskatchewan and Alberta)

NAME	TIME OF BLOOM (Hay-Fever Season)
Black Walnut *(Juglans nigra)*	March - May
***Cottonwood** *(Populus macdougali)*	**March - May**
Shad Scale *(Atriplex canescens)*	March - June
Oak *(Quercus alba)*	April - May
Rabbit Bush *(Franseria deltoidea)*	April - May
***Sweet Vernal Grass** *(Anthoxanthum odoratum)*	**April - July**
Orchard Grass *(Dactylis glomerata)*	April - Aug.
Sheep Sorrel *(Rumex acetosella)*	May - July
Yellow Dock *(Rumex crispus)*	May - July
***June Grass** *(Poa pratensis)*	**May - Sept.**
Timothy *(Phleum pratense)*	June - Aug.
***Lambs Quarters** *(Chenopodium album)*	**June - Sept.**
***Annual Saltbush** *(Atriplex Wrightii)*	**July - Sept.**
***Redroot Pigweed** *(Amaranthus retroflexus)*	**July - Sept.**
***Sage Brush** *(Artemisia tridentata)*	**July - Sept.**
Cocklebur *(Xanthium canadense)*	July - Sept.
***Russian Thistle** *(Salsola pestifer)*	**July - Sept.**
Mugwort *(Artemisia vulgaris)*	July - Oct.
***Summer Cypress** *(Kochia scoparia)*	**July - Oct.**
***Green Sage** *(Artemisia campestris)*	**July - Oct.**
***Pasture Sage** *(Artemisia frigida)*	**July - Oct.**
Ragweed *(Ambrosia elatior)*	Aug. - Oct.
Giant Ragweed *(Ambrosia trifida)*	Aug. - Oct.
***Western Ragweed** *(Ambrosia psilostachya)*	**Aug. - Oct.**
Slender Ragweed *(Franseria tenuifolia)*	Sept. - Oct.

*Pollens of primary importance.

For index of States and Provinces see page 44.

Southwestern States

(Southwestern Texas, New Mexico, Arizona, Southeastern California)

NAME	TIME OF BLOOM (Hay-Fever Season)
Mountain Cedar *(Juniperus sabinoides)*	Dec. - Feb.
***Cottonwood** *(Populus macdougali)* -	**Feb. - April**
Arizona Walnut *(Juglans major)* - -	March - May
Arizona Ash *(Fraximus toumeyi)* - -	March - May
***Shad Scale** *(Atriplex canescens)* - -	March - June
Oak *(Quercus alba)* - - - - - - -	April - May
***Rabbit Bush** *(Franseria deltoidea)* -	**April - May**
Olive *(Olea europaea)* - - - - - -	April - May
Sheep Sorrel *(Rumex acetosella)* - -	May - July
Yellow Dock *(Rumex crispus)* - - -	May - July
***June Grass** (Blue Grass, *Poa pratensis)* - - - - - - - - - - - -	**May - Sept.**
***Bermuda Grass** *(Capriola dactylon)*	**May - Sept.**
Lambs Quarters *(Chenopodium album)*	June - Sept.
Johnson Grass *(Sorghum halepense)* -	June - Oct.
***Annual Saltbush** *(Atriplex Wrightii)*	**July - Sept.**
***Redroot Pigweed** *(Amaranthus retroflexus)* - - - - - - - - - - - -	**July - Sept.**
Sage Brush *(Artemisia tridentata)* -	July - Sept.
Cocklebur *(Xanthium canadense)* - -	July - Sept.
***Russian Thistle** *(Salsola pestifer)* -	**July - Sept.**
***Careless Weed** *(Amaranthus palmeri)*	**July - Oct.**
Green Sage *(Artemisia campestris)* -	July - Oct.
Pasture Sage *(Artemisia frigida)* - -	July - Oct.
Western Water Hemp *(Acnida tamariscina)* - - - - - - - - - - - -	July - Oct.
Marsh Elder *(Iva ciliata)* - - - -	Aug. - Oct.
Western Ragweed *(Ambrosia psilostachya)* - - - - - - - - - - -	Aug. - Oct.
***Slender Ragweed** *(Franseria tenuifolia)* - - - - - - - - - - - - -	**Sept. - Oct.**
Southwestern Ragweed *(Ambrosia aptera)* - - - - - - - - - - - -	Sept. - Oct.

*Pollens of primary importance.

For index of States and Provinces see page 44.

Pacific States

(Nevada, California, Oregon, Washington)

(Canadian Province: British Columbia)

NAME	TIME OF BLOOM (Hay-Fever Season)
Cottonwood *(Populus macdougali)*	**Feb. - April**
***Black Walnut** *(Juglans nigra)*	March - May
Shad Scale *(Atriplex canescens)*	March - June
Oak *(Quercus alba)*	April - May
Rabbit Bush *(Franseria deltoidea)*	April - May
Olive *(Olea europaea)*	April - May
Sweet Vernal Grass *(Anthoxanthum odoratum)*	April - July
***Orchard Grass** *(Dactylis glomerata)*	April - Aug.
***Perennial Rye Grass** *(Lolium perenne)*	**May - July**
Sheep Sorrel *(Rumex acetosella)*	May - July
Yellow Dock *(Rumex crispus)*	May - July
***June Grass** (Blue Grass, *Poa pratensis)*	**May - Sept.**
***Bermuda Grass** *(Capriola dactylon)*	**May - Sept.**
***Timothy** *(Phleum pratense)*	**June - Aug.**
***Redtop** *(Agrostis palustris)*	**June - Sept.**
Lambs Quarters *(Chenopodium album)*	June - Sept.
***Johnson Grass** *(Sorghum halepense)*	**June - Oct.**
Annual Saltbush *(Atriplex Wrightii)*	July - Sept.
***Redroot Pigweed** *(Amaranthus retroflexus)*	**July - Sept.**
***Sage Brush** *(Artemisia tridentata)*	**July - Sept.**
Cocklebur *(Xanthium canadense)*	July - Sept.
***Russian Thistle** *(Salsola pestifer)*	**July - Sept.**
***Mugwort** *(Artemisia vulgaris)*	**July - Oct.**
***Careless Weed** *(Amaranthus palmeri)*	**July - Oct.**
Western Ragweed *(Ambrosia psilostachya)*	Aug. - Oct.
Slender Ragweed *(Franseria tenuifolia)*	Sept. - Oct.

*Pollens of primary importance.

For index of States and Provinces see page 44.

The State of California may be sub-divided into three sections and the pollens of primary importance in these districts are as follows:

San Francisco Bay District

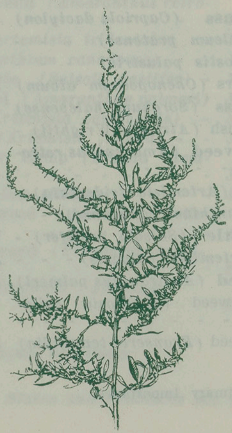
Black Walnut, Orchard Grass, Perennial Rye Grass, June Grass, Bermuda Grass, Redroot Pigweed, Sagebrush, Mugwort.

Sacramento and San Joaquin Valleys

Olive, Black Walnut, Orchard Grass, Perennial Rye Grass, June Grass, Bermuda Grass, Redtop, Johnson Grass, Redroot Pigweed, Mugwort.

Los Angeles-Pasadena District

Olive, Black Walnut, Orchard Grass, Perennial Rye Grass, June Grass, Bermuda Grass, Johnson Grass, Redroot Pigweed, Mugwort, Careless Weed.



Annual Saltbush
(Atriplex Wrightii)

Southwestern Area

As pointed out by WATSON and KIBLER,[11] the hay-fever problem in the Southwest is different and more complex than in the other geographical sections of the country, owing to the difference in climatic conditions. Rabbit bush and shad scale are probably the most important plants causing the spring type of hay-fever. Bermuda grass causes spring, summer and fall type of hay-fever at altitudes up to 4,500 feet and June grass (Bluegrass) above that altitude. The principal cause of fall hay-fever is usually careless weed, but some seasons this is replaced by annual saltbush. A less important cause of fall hay-fever is the slender ragweed.

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[11] WATSON, S. H., & KIBLER, C. S.: Etiology of Hay-Fever in Arizona and the Southwest, *Jour. A. M. A.*, Mar. 11, 1922, p. 719.

Black Walnut blossoms
(Juglans nigra)

CHAPTER VII

List of Hay-Fever Plants

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Arizona Walnut *(Juglans major)*	
Bermuda Grass *(Capriola dactylon)*	12
Black Walnut *(Juglans nigra)*	39
Careless Weed *(Amaranthus palmeri)*	21
Cocklebur *(Xanthium canadense)*	27
Cottonwood *(Populus macdougali)*	6
Grass, Bermuda *(Capriola dactylon)*	12
Grass, Johnson *(Sorghum halapense)*	5
Grass, June *(Poa pratensis)*	11
Grass, Orchard *(Dactylis glomerata)*	7
Grass, Perennial Rye *(Lolium parenne)*	10
Grass, Redtop *(Agrostis palustris)*	19
Grass, Sweet Vernal *(Anthoxanthum odoratum)*	1
Grass, Timothy *(Phleum pratense)*	16
Green Sage *(Artemisia campestris)*	18
Giant Ragweed *(Ambrosia trifida)*	26
Johnson Grass *(Sorghum halapense)*	5
June Grass *(Poa pratensis)*	11
Lambs Quarters *(Chenopodium album)*	4
Marsh Elder *(Iva ciliata)*	28
Mountain Cedar *(Juniperus sabinoides)*	11
Mugwort *(Artemisia vulgaris)*	26

(List continued on next page)

See tables on pages 30 to 39 for relative importance of the hay-fever plants in various sections of the country.

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Rabbit Bush *(Franseria deltoidea)*	24
Ragweed *(Ambrosia elatior)*	22
Ragweed, Giant *(Ambrosia trifida)*	26
Ragweed, Slender *(Franseria tenuifolia)*	22
Ragweed, Southwestern *(Ambrosia aptera)*	23
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Redroot Pigweed *(Amaranthus retroflexus)*	29
Redtop *(Agrostis palustris)*	19
Russian Thistle *(Salsola pestifer)*	25
Sage Brush *(Artemisia tridentata)*	28
Sage, Green *(Artemisia campestris)*	18
Sage, Pasture *(Artemisia frigida)*	17
Shad Scale *(Atriplex canescens)*	14
Sheep Sorrel *(Rumex acetosella)*	13
Slender Ragweed *(Franseria tenuifolia)*	22
Southwestern Ragweed *(Ambrosia aptera)*	23
Spiny Amaranth *(Amaranthus spinosus)*	18
Summer Cypress *(Kochia scoparia)*	
Sweet Vernal Grass *(Anthoxanthum odoratum)*	1
Timothy *(Phleum pratense)*	16
Walnut, Arizona *(Juglans major)*	
Walnut, Black *(Juglans nigra)*	39
Western Ragweed *(Ambrosia psilostachya)*	3
Western Water Hemp *(Acnida tamariscina)*	14
Yellow Dock *(Rumex crispus)*	15

See tables on pages 30 to 39 for relative importance of the hay-fever plants in various sections of the country.

Botanical Species of Hay-Fever Plants With Their Common English Names

Pollens from the following species are used in the preparation of Pollen Antigens (Lederle):

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Franseria deltoidea (Rabbit Bush) 24
Franseria tenuifolia (Slender Ragweed) . . 22
Fraxinus toumeyi (Arizona Ash) 20
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Juglans nigra (Black Walnut) 39
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Kochia scoparia (Summer Cypress, Fireball, Burning Bush)
Lolium perenne (Perennial Rye Grass, Australian Rye Grass) 10
Olea europaea (Olive)
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Poa pratensis (June Grass, Kentucky Bluegrass) 11
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